

#### REMARKS

Reconsideration of this application is respectfully requested.

Claims 283-362, 364-380, 382-398, 400-404, 406-439 and 441-463 were previously pending in this application. Claims 283-290, 312, 318, 330, 360-361, 411 and 413-414 have been amended. Claims 464-505 have been added and no claims have been canceled. Accordingly, claims 283-362, 364-380, 382-398, 400-404, 406-439 and 441-505 are presented for further examination on the merits.

Before discussing the above changes to the claims and addressing the issues in the June 22, 1998 Office Action, Applicants would like to acknowledge their appreciation that several claims have been allowed by the Examiner and that several other claims are indicated to be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims. Applicants further appreciate that several issues including new matter under 35 U.S.C. §112, first paragraph, and indefiniteness under 35 U.S.C. §112, second paragraph, have been withdrawn in the latest Office Action.

In a sincere effort to advance prosecution, Applicants have amended the claims as follows. **First**, in response to the rejection under the fourth paragraph of 35 U.S.C. §112, Applicants have amended claims 312, 318 and 330 in order to correct a problem with improper dependent form. The Examiner had astutely observed that each of these claims failed to further limit the subject matter of a previous claim. Thus, the dependencies have been changed and the word "modified" has been deleted from all three claims. It is believed that these claims are now of proper dependent form in that each limits the subject matter of a previous claim, the previous claims being claims 310, 316 and 327 in the case of claims 312, 318 and 330, respectively. **Second**, the main independent claims for the compositions and the kit claims have been amended by the insertion of the term "non-radioactive" before each instance where a signal generating portion(s) is/are recited. The claims affected by this amendment include composition claims 283-290, article of manufacture claims 360-361 and kit claims 411 and 413-414.

**Third**, Applicants have added new claims 464-487 in order to act upon the

Examiner's indication of allowable subject matter with respect to several claims which were objected to as being dependent upon a rejected base claim. The objected claims included claims 297, 302, 303, 305, 306, 308, 322, 334, 341-346, 348, 349, 351, 352, 354-357, 420, 421, 426-431, 434 and 435. Many if not most of these claims depended from several other base claims. For example, twelve claims, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293 and 294, are recited numerous times as the base claims to several of the objected claims. In redrafting the objected claims into independent form, Applicants took the liberty of adding new independent claims 464-475, corresponding to the twelve base claims, and to these new claims, a number of embodiments were incorporated as Markush members. These include the nature of the analyte or molecularly recognizable portion on the analyte, the first portion of the molecular bridging entity and the signal generating portion or chemically modified or artificially altered polynucleotides, the latter two of which are capable of directly or indirectly providing a detectable signal. Thus, rewritten in the independent form of new claims 464-475 are the limitations of claims 297 with respect to the analyte, the limitations of claims 302, 303, 305, 306 and 308 with respect to the molecular bridging entity first portion, the limitations of claim 322 for the molecular bridging entity second portion, the limitations of claim 334 with respect to the signalling entity nucleic acid portion, and the limitations of 341-346 with respect to the signal generating portion. In addition, the subject matter wherein nucleic acid sequences or segments are derived from various phage members is recited as new dependent 476. Further, the subject matter defining various ratios of elements previously found in claims 348, 349, 351, 352 and 354-357 can now be found in new dependent claims 477 and 478.

In new kit claims 479-485, the ratios of various elements are incorporated as Markush members. In this way, claims 420, 421 and 426-431 have been rewritten in independent form. Finally, with respect to the object claims, the limitations of claims 434 and 435 with respect to the signal generating portion(s) and the chemically modified or artificially altered polynucleotides can now be found in new dependent claims 486 and 487.

Lastly, commensurate with their complete and broad disclosure, and in response to the latest Office Action, Applicants are presenting new claims 488-505 which are directed to kit claims for carrying out the process defined by the allowed

process claims. The latter include process claims 443-460. New kit claim 488 defines, for example, "[a] kit for use in carrying out the process of claim 443, said kit comprising as components thereof the first part and the second part of the composition provided in said process." It is believed that because the process claims have been allowed, that kits specifically designed for use with such processes are also allowable. Entry of new claims 488-505 is respectfully urged.

Before turning to the substantive issues in the Office Action at hand, Applicants wish to point out that they are filing concurrently with this Amendment a Request Under 37 C.F.R. §1.129(a) For Withdrawal Of The Finality Of The June 22, 1998 Office Action and authorization for the fee therefor.

**The Rejection Under 35 U.S.C. §112, Fourth Paragraph**

Claims 312, 318 and 330 stand rejected under 35 U.S.C. §112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim. As astutely noted by the Examiner on page 2 of the Office Action, "[c]laims 312, 318 and 330 cite all options for modifications and thus fail to further limit the claims from which they depend."

As indicated in their opening remarks above, in addition to the deletion of the word "modified," the dependencies in all three claims have been changed. Claims 312, 318 and 330 now depend from claims 310, 316 and 327, respectively. It is believed that the foregoing amendments obviates the rejection for improper dependent form.

Reconsideration and withdrawal of the rejection under the fourth paragraph of 35 U.S.C. §112 is respectfully requested.

**The Rejection Under 35 U.S.C. §102(b)**

Claims 283-296, 298-301, 304, 307, 309-321, 323-333, 335-340, 347, 350, 353, 358-362, 411, 413, 414, 416, 418, 419, 422-425, 432, 436-438, 441 and 461-463 stand rejected under 35 U.S.C. §102(b) for anticipation by Dunn

et al. ["A Novel Method to Map Transcripts: Evidence for Homology between an Adenovirus mRNA and Discrete Multiple Regions of the Viral Genome," *Cell* 12:23-36 (1977)]. In the Office Action (pages 3-4), the Examiner stated:

This rejection is maintained and reiterated from the previous office action, mailed 10/27/97, only regarding the instant composition claims and necessitated by amendment regarding the newly added claims. This will be discussed below. Firstly, the withdrawal of the instant detection method claims from this rejection is based on the persuasive arguments of applicants and the Declaration of Dr. Wetmur as to what is characterized as the analyte or target in the method of Dunn et al. or sandwich hybridization assays such as that of Ranki et al. (P/N 4,486,539). For example, in instant claim 442 the analyte detection conclusion is drawn from the signal produced by the signalling entity. This analyte is not hybridized between two polynucleotide probes but rather only specifically hybridized to the bridging polynucleotide which in turn is specifically hybridized to the signalling polynucleotide at another segment within the bridging entity. In such methods the entity referred to as the analyte or target is related to the signal and therefore its location within the sandwich is critical. Turning back to the composition claims, the analysis is not the same. Composition claim subject matter is exactly that. It is a composition. In the instant claim 283, for example, two polynucleotides are claimed with certain hybridization characteristics. Three entities are described so as to define these hybridization characteristics. These are the analyte, molecular bridging entity, and the signalling entity(ies). When the composition is, however, viewed as to what it actually is, it is at least two polynucleotides with specific hybridization capabilities to other specific polynucleotides. Such specificity of hybridization to certain polynucleotides is also a characteristic of polynucleotides of Dunn et al. The naming of these polynucleotides as analyte, bridging, and signalling entities convey patentable distinctness over polynucleotides with the same specificity characteristics such as given in Dunn et al., although naming the polynucleotides differently. If naming entities alone within composition claims conveyed patentable distinctness, while acknowledging that sequence specificity and any other characteristics, for example, are the same, then naming the polynucleotides of such a composition with novel names would result in patentability. Clearly, this would be unreasonable and generate undue confusion because novel names can be generated at will if desired. In summary, the instant composition claims, kit claims, and articles of manufacture citing the same compositions are still deemed properly rejected hereinunder.

The anticipation rejection is respectfully traversed.

In response, Applicants would respectfully like to point out that the instant composition, article of manufacture and kit claims wherein a signal generating portion is recited therein (claims 283-290, 360, 411 and 413-414) now specifically

calls for that element to be "non-radioactive." With respect to other composition and kit claims wherein one or more chemically modified or artificially altered polynucleotides are recited (claims 291-294, 361 and 484-485), it is respectfully submitted that the subject matter of these claims *per se* are deemed to be outside of Dunn's disclosure for the simple reason and fact that radioisotopic labeling of the nucleic acid phosphate with  $^{32}\text{P}$  does not constitute a chemical modification or artificial alteration as defined by the instant claims. Radioisotopic labelling of nucleic acid probes using  $^{32}\text{P}$  is well recognized in the art as being based on the mere exchange or substitution of a hot isotopic marker. Unlike the instantly defined invention, no chemical modification or artificial alteration of the nucleic acid resulted from Dunn's radioisotopic labelling with  $^{32}\text{P}$ .

In light of the above amendments to the claims and the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the anticipation rejection.

#### **The Objection for Improper Dependent Form**

Claims 297, 302, 303, 305, 306, 308, 322, 334, 341-346, 348, 349, 351, 352, 354-357, 420, 421, 426-431, 434 and 435 were objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

As indicated in their opening remarks to this Amendment, Applicants have largely rewritten the objected claims in independent form, or if not in independent form, then depending from new independent claims with limitations that are believed to render such claims allowable. The claims in rewritten form include claims 464-487.

Applicants respectfully request entry of new claims 464-487 and an indication of their allowability.

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#### SUMMARY AND CONCLUSIONS

Claims 283-362, 364-380, 382-398, 400-404, 406-439 and 441-505 are presented for further examination on the merits. Claims 283-290, 312, 318, 330, 360-361, 411 and 413-414 have been amended. Claims 464-505 have been added and no claims have been canceled. No new matter has been inserted by any of the foregoing amendments or added claims.

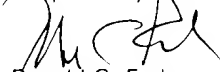
The cost for presenting the claims above is believed to be \$3,076, based upon an additional nineteen (19) new independent claims and forty-two (42) dependent claims being presented hereinabove. In addition, twenty-seven (27) dependent claims are presented by virtue of multiple dependent claims, the fee for presenting multiple dependent claims having been previously paid in this application.

The Patent and Trademark Office is hereby authorized to charge the amount of \$3,076 to Deposit Account No. 05-1135, based upon the presentation of the 19 new independent claims ( $19 \times \$82 = \$1,558$  for a large entity) and 69 dependent claims ( $69 \text{ claims} \times \$22 = \$1,518$  for a large entity). If any other fee or fees are due in connection with this Amendment or the Request Under 37 C.F.R. §1.129(a) For Withdrawal Of The Finality Of The June 22, 1998 Office Action, authorization is further hereby given to charge the amount of any such other fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If it would be helpful to expediting the prosecution of this application, the undersigned may be contacted by telephone at 212-583-0100 during the daytime business hours.

Early and favorable action on this application is respectfully sought.

Respectfully submitted



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